

**WHAT IS CLAIMED IS:**

- 1           1.     A method of manufacturing a family of antigenic peptides comprising:  
2           locating a plurality of variable positions in a region of a pathogen protein;  
3           choosing a peptide sequence of the pathogen protein including the plurality of  
4           variable positions;  
5           selecting one or more substitute amino acid residues for one of the variable positions  
6           based on antigenic similarity to amino acid residues naturally occurring at the variable  
7           position of the pathogen protein; and  
8           preparing a family of antigenic peptides based on the peptide sequence and including  
9           the substitute amino acid residues.
- 1           2.     The method of claim 1, wherein selecting includes determining the antigenic  
2           similarity using an antigenic similarity matrix.
- 1           3.     The method of claim 1, further comprising assigning a frequency to each  
2           substitute amino acid residue in the family of antigenic peptides.
- 1           4.     The method of claim 3, wherein preparing includes weighting the substitute  
2           amino acid residues in the family of antigenic peptides based on the assigned frequency.
- 1           5.     The method of claim 3, wherein assigning further includes considering the  
2           frequency with which the variations naturally occur.
- 1           6.     The method of claim 1, wherein the pathogen protein includes a hypervariable  
2           region.
- 1           7.     The method of claim 1, wherein the pathogen protein is associated with a  
2           virus.
- 1           8.     The method of claim 7, wherein the virus is HIV.
- 1           9.     The method of claim 1, wherein the pathogen protein is HIV gp120.

1           10.     The method of claim 9, wherein the region is selected from the group  
2     consisting of the V1, V2, V3, V4, and V5 regions.

1           11.     The method of claim 7, wherein the virus is hepatitis B virus or hepatitis C  
2     virus.

1           12.     The method of claim 7, wherein the virus is an influenza virus.

1           13.     The method of claim 7, wherein the virus is a dengue virus.

1           14.     The method of claim 1, wherein the pathogen protein is associated with a  
2     malaria pathogen.

1           15.     The method of claim 1, wherein the pathogen protein is associated with a  
2     tuberculosis pathogen.

1           16.     The method of claim 1, further comprising determining an antigenic similarity  
2     between a peptide of the family and a region of a human protein.

1           17.     The method of claim 16, further comprising removing a peptide from the  
2     family of antigenic peptides before preparing the family if the determined antigenic similarity  
3     between the peptide of the family and the region of a human protein exceeds a predetermined  
4     threshold.

1           18.     The method of claim 1, wherein the family of antigenic peptides includes  
2     members, such that the members taken together have antigenic similarity to each naturally  
3     occurring sequence of the region of the pathogen protein.

1           19.     The method of claim 1, wherein the family of antigenic peptides includes  
2     members, such that the members taken together have antigenic similarity to a non-naturally  
3     occurring sequence of the region of the pathogen protein.

1           20.     The method of claim 1, further comprising identifying peptide sequences of  
2     the family, the identified peptide sequences being representative of the sequence diversity of  
3     the entire family.

1           21.     The method of claim 20, wherein fewer than 500 sequences are identified.

1           22.     The method of claim 20, wherein identifying includes calculating a distance  
2 between peptide sequences of the family.

1           23.     The method of claim 22, wherein calculating a distance includes using an  
2 antigenic similarity matrix.

1           24.     The method of claim 1, wherein preparing the family of antigenic peptides  
2 includes chemical synthesis of the family of peptides.

1           25.     The method of claim 24, wherein the chemical synthesis includes  
2 combinatorial synthesis, whereby the peptides are formed as a mixture of different  
3 sequences.

1           26.     The method of claim 24, wherein the chemical synthesis includes parallel  
2 synthesis, whereby each peptide is formed separately from other peptides.

1           27.     The method of claim 26, further comprising mixing the separate peptides.

1           28.     The method of claim 1, wherein preparing the family of antigenic peptides  
2 includes expression of the family of peptides by a host organism.

1           29.     A composition comprising a family of antigenic peptides having amino acid  
2 sequences having antigenic similarity to amino acid sequences of a variable region of a  
3 pathogen protein, wherein each antigenic peptide in the family has at least one amino acid  
4 position that varies relative to other antigenic peptides in the family.

1           30.     The composition of claim 29, wherein one amino acid residue occurs more  
2 frequently than another in the position that varies.

1           31.     The composition of claim 29, wherein the family includes greater than 150  
2 mutually unique antigenic peptides.

1           32.     The composition of claim 29, wherein the family includes greater than 1,000  
2 mutually unique antigenic peptides.

1           33.     The composition of claim 29, wherein the family includes fewer than 100,000  
2 mutually unique antigenic peptides.

1           34.     The composition of claim 29, wherein the family includes fewer than 50,000  
2 mutually unique antigenic peptides.

1           35.     The composition of claim 29, wherein the family includes between 1,000 and  
2 50,000 mutually unique antigenic peptides.

1           36.     The composition of claim 29, wherein the pathogen protein is HIV gp120.

1           37.     The composition of claim 36, wherein the variable region is selected from the  
2 group consisting of the V1 region, the V2 region, the V3 region, the V4 region and the V5  
3 region.

1           38.     The composition of claim 37, wherein the family of antigenic peptides  
2 includes sequences having antigenic similarity to sequences from a subtype of HIV.

1           39.     The composition of claim 38, wherein the subtype is selected from the group  
2 consisting of subtype A, subtype B, subtype C, subtype D, subtype F, subtype G, a  
3 recombinant subtype, a subtype of HIV group N, a subtype of HIV group O, and  
4 combinations thereof.

1           40.     The composition of claim 29, wherein at least two members of the family of  
2 antigenic peptides are mixed together.

1           41.     The composition of claim 29, wherein the family of antigenic peptides are  
2 separated according to sequence.

1           42.     The composition of claim 29, wherein the family includes a multiple antigenic  
2 peptide.

1           43.     A peptide library comprising a family of peptides including the fragment:  
2           -N-N-T-R-X<sup>4</sup>-X<sup>5</sup>-X<sup>6</sup>-X<sup>7</sup>-X<sup>8</sup>-G-X<sup>9</sup>-G-X<sup>10</sup>-X<sup>11</sup>-X<sup>12</sup>-X<sup>13</sup>-X<sup>14</sup>-T-G-X<sup>15</sup>-I-X<sup>16</sup>-G-X<sup>17</sup>-I-R-  
3 wherein each X<sup>4</sup>-X<sup>17</sup> is a fragment zero, one, two or three amino acid residues in length.

1           44.     The peptide library of claim 43, wherein the family has antigenic similarity to  
2     the V3 region of HIV gp120.

1           45.     The peptide library of claim 44, wherein the family has antigenic similarity to  
2     the V3 region of HIV gp120 of HIV subtypes A, B, C, D, F, and G.

1           46.     The peptide library of claim 43, wherein the family of peptides have the  
2     formula:

3            $X^1-C-X^2-R-P-X^3-N-N-T-R-X^4-X^5-X^6-X^7-X^8-G-X^9-G-X^{10}-X^{11}-X^{12}-X^{13}-X^{14}-T-G-X^{15}-I-X^{16}-G-X^{17}-I-R-$   
4      $X^{18}-A-X^{19}-C-X^{20}$

5     wherein each  $X^1-X^{20}$  is a fragment zero, one, two or three amino acid residues in length.

1           47.     The peptide library of claim 46, wherein for each peptide of the family,  $X^1$   
2     independently is N, V, T or E.

1           48.     The peptide library of claim 46, wherein for each peptide of the family,  $X^2$   
2     independently is T or I.

1           49.     The peptide library of claim 46, wherein for each peptide of the family,  $X^3$   
2     independently is N, S, G or Y.

1           50.     The peptide library of claim 46, wherein for each peptide of the family,  $X^4$   
2     independently is K, Q or T.

1           51.     The peptide library of claim 46, wherein for each peptide of the family,  $X^5$   
2     independently is S, G or R.

1           52.     The peptide library of claim 46, wherein for each peptide of the family,  $X^6$   
2     independently is I, T or M.

1           53.     The peptide library of claim 46, wherein for each peptide of the family,  $X^7$   
2     independently is H, R, P, S or N.

1           54.     The peptide library of claim 46, wherein for each peptide of the family,  $X^8$   
2     independently is I or M.

1           55.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>9</sup>  
2 independently is P or L.

1           56.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>10</sup>  
2 independently is R or Q.

1           57.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>11</sup>  
2 independently is A, T or V.

1           58.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>12</sup>  
2 independently is F or W.

1           59.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>13</sup>  
2 independently is Y, F or H.

1           60.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>14</sup>  
2 independently is A or T.

1           61.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>15</sup>  
2 independently is D, Q, A or R.

1           62.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>16</sup>  
2 independently is I or T.

1           63.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>17</sup>  
2 independently is D or N.

1           64.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>18</sup>  
2 independently is Q or K.

1           65.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>19</sup>  
2 independently is H or Y.

1           66.    The peptide library of claim 46, wherein for each peptide of the family, X<sup>20</sup>  
2 independently is N or T.

1           67.     The peptide library of claim 46, wherein for each peptide of the family, X<sup>1</sup>  
 2 independently is N, V, T or E; X<sup>2</sup> independently is T or I; X<sup>3</sup> independently is N, S, G or Y;  
 3 X<sup>4</sup> independently is K, Q or T; X<sup>5</sup> independently is S, G or R; X<sup>6</sup> independently is I, T or M;  
 4 X<sup>7</sup> independently is H, R, P, S or N; X<sup>8</sup> independently is I or M; X<sup>9</sup> independently is P or L;  
 5 X<sup>10</sup> independently is R or Q; X<sup>11</sup> independently is A, T or V; X<sup>12</sup> independently is F or W;  
 6 X<sup>13</sup> independently is Y, F or H; X<sup>14</sup> independently is A or T; X<sup>15</sup> independently is D, Q, A or  
 7 R; X<sup>16</sup> independently is I or T; X<sup>17</sup> independently is D or N; X<sup>18</sup> independently is Q or K; X<sup>19</sup>  
 8 independently is H or Y; and X<sup>20</sup> independently is N or T.

1           68.     The peptide library of claim 46, wherein at least two members of the family of  
 2 peptides are mixed together.

1           69.     The peptide library of claim 46, wherein the family of peptides are separated  
 2 according to sequence.

1           70.     The peptide library of claim 46, wherein the family includes greater than 150  
 2 mutually unique peptide sequences.

1           71.     The peptide library of claim 46, wherein the family includes fewer than  
 2 100,000 mutually unique peptide sequences.

1           72.     The peptide library of claim 46, wherein the family includes fewer than 500  
 2 mutually unique peptide sequences, the sequences being representative of the entire sequence  
 3 diversity available.

1           73.     A peptide library comprising a family of peptides including the fragment:  
 2 -N-N-X<sup>4</sup>-R-X<sup>5</sup>-X<sup>6</sup>-V-X<sup>7</sup>-I-G-P-G-X<sup>8</sup>-X<sup>9</sup>-F-X<sup>10</sup>-X<sup>11</sup>-X<sup>12</sup>-X<sup>13</sup>-X<sup>14</sup>-I-X<sup>15</sup>-G-X<sup>16</sup>-I-R-  
 3 wherein each X<sup>4</sup>-X<sup>16</sup> is a fragment zero, one, two or three amino acid residues in length.

1           74.     The peptide library of claim 73, wherein the family has antigenic similarity to  
 2 the V3 region of HIV gp120.

1           75.     The peptide library of claim 74, wherein the family has antigenic similarity to  
 2 the V3 region of HIV gp120 of HIV subtype A.

1           76.    The peptide library of claim 73, wherein the family of peptides have the  
2 formula:

3                    $X^1-C-X^2-R-P-X^3-N-N-X^4-R-X^5-X^6-V-X^7-I-G-P-G-X^8-X^9-F-X^{10}-X^{11}-X^{12}-X^{13}-X^{14}-I-X^{15}-G-X^{16}-I-R-$   
4  $X^{17}-A-X^{18}-C-X^{19}$

5 wherein each  $X^1-X^{19}$  is a fragment zero, one, two or three amino acid residues in length.

1           77.    The peptide library of claim 76, wherein for each peptide of the family,  $X^1$   
2 independently is N, T, or D.

1           78.    The peptide library of claim 76, wherein for each peptide of the family,  $X^2$   
2 independently is T or I.

1           79.    The peptide library of claim 76, wherein for each peptide of the family,  $X^3$   
2 independently is N, G, or S.

1           80.    The peptide library of claim 76, wherein for each peptide of the family,  $X^4$   
2 independently is T or K.

1           81.    The peptide library of claim 76, wherein for each peptide of the family,  $X^5$   
2 independently is K, T, or Q.

1           82.    The peptide library of claim 76, wherein for each peptide of the family,  $X^6$   
2 independently is S, G, R or N.

1           83.    The peptide library of claim 76, wherein for each peptide of the family,  $X^7$   
2 independently is R or H.

1           84.    The peptide library of claim 76, wherein for each peptide of the family,  $X^8$   
2 independently is Q or R.

1           85.    The peptide library of claim 76, wherein for each peptide of the family,  $X^9$   
2 independently is A, T, or V.

1           86.    The peptide library of claim 76, wherein for each peptide of the family,  $X^{10}$   
2 independently is Y, F, or H.



1           87.    The peptide library of claim 76, wherein for each peptide of the family, X<sup>11</sup>  
2 independently is A or T.

1           88.    The peptide library of claim 76, wherein for each peptide of the family, X<sup>12</sup>  
2 independently is T, R, A, or no residue.

1           89.    The peptide library of claim 76, wherein for each peptide of the family, X<sup>13</sup>  
2 independently is G, D, or no residue.

1           90.    The peptide library of claim 76, wherein for each peptide of the family, X<sup>14</sup>  
2 independently is D, A, N, R, or V.

1           91.    The peptide library of claim 76, wherein for each peptide of the family, X<sup>15</sup>  
2 independently is I or T.

1           92.    The peptide library of claim 76, wherein for each peptide of the family, X<sup>16</sup>  
2 independently is D or N.

1           93.    The peptide library of claim 76, wherein for each peptide of the family, X<sup>17</sup>  
2 independently is Q, K, or E.

1           94.    The peptide library of claim 76, wherein for each peptide of the family, X<sup>18</sup>  
2 independently is H or Y.

1           95.    The peptide library of claim 76, wherein for each peptide of the family, X<sup>19</sup>  
2 independently is N, T, or E.

1           96.    The peptide library of claim 76, wherein for each peptide of the family X<sup>1</sup>  
2 independently is N, T, or D; X<sup>2</sup> independently is T or I; X<sup>3</sup> independently is N, G, or S; X<sup>4</sup>  
3 independently is T or K; X<sup>5</sup> independently is K, T, or Q; X<sup>6</sup> independently is S, G, R or N;  
4 X<sup>7</sup> independently is R or H; X<sup>8</sup> independently is Q or R; X<sup>9</sup> independently is A, T, or V; X<sup>10</sup>  
5 independently is Y, F, or H; X<sup>11</sup> independently is A or T; X<sup>12</sup> independently is T, R, A, or no  
6 residue; X<sup>13</sup> independently is G, D, or no residue; X<sup>14</sup> independently is D, A, N, R, or V; X<sup>15</sup>  
7 independently is I or T; X<sup>16</sup> independently is D or N; X<sup>17</sup> independently is Q, K, or E; X<sup>18</sup>  
8 independently is H or Y; and X<sup>19</sup> independently is N, T, or E.

1           97.    The peptide library of claim 76, wherein at least two members of the family of  
2 peptides are mixed together.

1           98.    The peptide library of claim 76, wherein the family of peptides are separated  
2 according to sequence.

1           99.    The peptide library of claim 76, wherein the family includes greater than 150  
2 mutually unique peptide sequences.

1           100.   The peptide library of claim 76, wherein the family includes fewer than  
2 100,000 mutually unique peptide sequences.

1           101.   The peptide library of claim 76, wherein the family includes fewer than 500  
2 mutually unique peptide sequences, the sequences being representative of the entire sequence  
3 diversity available.

1           102.   A peptide library comprising a family of peptides including the fragment:  
2 -N-N-T-R-K-X<sup>4</sup>-I-X<sup>5</sup>-X<sup>6</sup>-G-X<sup>7</sup>-G-X<sup>8</sup>-X<sup>9</sup>-X<sup>10</sup>-X<sup>11</sup>-X<sup>12</sup>-T-X<sup>13</sup>-X<sup>14</sup>-I-X<sup>15</sup>-G-X<sup>16</sup>-I-R-  
3 wherein each X<sup>4</sup>-X<sup>16</sup> is a fragment zero, one, two or three amino acid residues in length.

1           103.   The peptide library of claim 102, wherein the family has antigenic similarity  
2 to the V3 region of HIV gp120.

1           104.   The peptide library of claim 103, wherein the family has antigenic similarity  
2 to the V3 region of HIV gp120 of HIV subtype B.

1           105.   The peptide library of claim 102, wherein the family of peptides have the  
2 formula:

3           X<sup>1</sup>-C-X<sup>2</sup>-R-P-X<sup>3</sup>-N-N-T-R-K-X<sup>4</sup>-I-X<sup>5</sup>-X<sup>6</sup>-G-X<sup>7</sup>-G-X<sup>8</sup>-X<sup>9</sup>-X<sup>10</sup>-X<sup>11</sup>-X<sup>12</sup>-T-X<sup>13</sup>-X<sup>14</sup>-I-X<sup>15</sup>-G-X<sup>16</sup>-I-R-  
4 X<sup>17</sup>-A-X<sup>18</sup>-C-X<sup>19</sup>  
5 wherein each X<sup>1</sup>-X<sup>19</sup> is a fragment zero, one, two or three amino acid residues in length.

1           106.   The peptide library of claim 105, wherein for each peptide of the family, X<sup>1</sup>  
2 independently is N, T, or H.

1           107. The peptide library of claim 105, wherein for each peptide of the family, X<sup>2</sup>  
2 independently is T or I.

1           108. The peptide library of claim 105, wherein for each peptide of the family, X<sup>3</sup>  
2 independently is N, S, or G.

1           109. The peptide library of claim 105, wherein for each peptide of the family, X<sup>4</sup>  
2 independently is S, G, or R.

1           110. The peptide library of claim 105, wherein for each peptide of the family, X<sup>5</sup>  
2 independently is H, P, N, T or Y.

1           111. The peptide library of claim 105, wherein for each peptide of the family, X<sup>6</sup>  
2 independently is I or M.

1           112. The peptide library of claim 105, wherein for each peptide of the family, X<sup>7</sup>  
2 independently is P, L, or W.

1           113. The peptide library of claim 105, wherein for each peptide of the family, X<sup>8</sup>  
2 independently is R, Q, G or S.

1           114. The peptide library of claim 105, wherein for each peptide of the family, X<sup>9</sup>  
2 independently is A, V or T.

1           115. The peptide library of claim 105, wherein for each peptide of the family, X<sup>10</sup>  
2 independently is F, W, or V.

1           116. The peptide library of claim 105, wherein for each peptide of the family, X<sup>11</sup>  
2 independently is Y, F or H.

1           117. The peptide library of claim 105, wherein for each peptide of the family, X<sup>12</sup>  
2 independently is T or A.

1           118. The peptide library of claim 105, wherein for each peptide of the family, X<sup>13</sup>  
2 independently is G, E or R.

1           119. The peptide library of claim 105, wherein for each peptide of the family, X<sup>14</sup>  
2 independently is E, Q, R or G.

1           120. The peptide library of claim 105, wherein for each peptide of the family, X<sup>15</sup>  
2 independently is I or T.

1           121. The peptide library of claim 105, wherein for each peptide of the family, X<sup>16</sup>  
2 independently is D or N.

1           122. The peptide library of claim 105, wherein for each peptide of the family, X<sup>17</sup>  
2 independently is Q or K.

1           123. The peptide library of claim 105, wherein for each peptide of the family, X<sup>18</sup>  
2 independently is H or Y.

1           124. The peptide library of claim 105, wherein for each peptide of the family, X<sup>19</sup>  
2 independently is N or T.

1           125. The peptide library of claim 105, wherein for each peptide of the family, X<sup>1</sup>  
2 independently is N, T or H; X<sup>2</sup> independently is T or I; X<sup>3</sup> independently is N, S, or G; X<sup>4</sup>  
3 independently is S, G, or R; X<sup>5</sup> independently is H, P, N, T or Y; X<sup>6</sup> independently is I or M;  
4 X<sup>7</sup> independently is P, L, or W; X<sup>8</sup> independently is R, Q, G or S; X<sup>9</sup> independently is A, V  
5 or T; X<sup>10</sup> independently is F, W, or V; X<sup>11</sup> independently is Y, F or H; X<sup>12</sup> independently is T  
6 or A; X<sup>13</sup> independently is G, E or R; X<sup>14</sup> independently is E, Q, R or G; X<sup>15</sup> independently is  
7 I or T; X<sup>16</sup> independently is D or N; X<sup>17</sup> independently is Q or K; X<sup>18</sup> independently is H or  
8 Y; and X<sup>19</sup> independently is N or T.

1           126. The peptide library of claim 105, wherein at least two members of the family  
2 of peptides are mixed together.

1           127. The peptide library of claim 105, wherein the family of peptides are separated  
2 according to sequence.

1           128. The peptide library of claim 105, wherein the family includes greater than 150  
2 mutually unique peptide sequences.

1 129. The peptide library of claim 105, wherein the family includes fewer than  
2 100,000 mutually unique peptide sequences.

1 130. The peptide library of claim 105, wherein the family includes fewer than 500  
2 mutually unique peptide sequences, the sequences being representative of the entire sequence  
3 diversity available.

1 131. A peptide library comprising a family of peptides including the fragment:  
2 -N-N-T-R-X<sup>4</sup>-X<sup>5</sup>-X<sup>6</sup>-X<sup>7</sup>-I-G-P-G-Q-X<sup>8</sup>-F-X<sup>9</sup>-X<sup>10</sup>-T-X<sup>11</sup>-X<sup>12</sup>-I-X<sup>13</sup>-G-X<sup>14</sup>-I-R-  
3 wherein each X<sup>4</sup>-X<sup>14</sup> is a fragment zero, one, two or three amino acid residues in length.

1 132. The peptide library of claim 131, wherein the family has antigenic similarity  
2 to the V3 region of HIV gp120.

1 133. The peptide library of claim 132, wherein the family has antigenic similarity  
2 to the V3 region of HIV gp120 of HIV subtype C.

1 134. The peptide library of claim 131, wherein the family of peptides have the  
2 formula:  
3 X<sup>1</sup>-C-X<sup>2</sup>-R-P-X<sup>3</sup>-N-N-T-R-X<sup>4</sup>-X<sup>5</sup>-X<sup>6</sup>-X<sup>7</sup>-I-G-P-G-Q-X<sup>8</sup>-F-X<sup>9</sup>-X<sup>10</sup>-T-X<sup>11</sup>-X<sup>12</sup>-I-X<sup>13</sup>-G-X<sup>14</sup>-I-R-X<sup>15</sup>-A-  
4 X<sup>16</sup>-C-X<sup>17</sup>  
5 wherein each X<sup>1</sup>-X<sup>17</sup> is a fragment zero, one, two or three amino acid residues in length.

1 135. The peptide library of claim 134, wherein for each peptide of the family, X<sup>1</sup>  
2 independently is V, N, E, T, M or R.

1 136. The peptide library of claim 134, wherein for each peptide of the family, X<sup>2</sup>  
2 independently is T, I, or A.

1 137. The peptide library of claim 134, wherein for each peptide of the family, X<sup>3</sup>  
2 independently is N, G, S, or H.

1 138. The peptide library of claim 134, wherein for each peptide of the family, X<sup>4</sup>  
2 independently is K, E or Q.

1           139. The peptide library of claim 134, wherein for each peptide of the family, X<sup>5</sup>  
2 independently is S or G.

1           140. The peptide library of claim 134, wherein for each peptide of the family, X<sup>6</sup>  
2 independently is I or M.

1           141. The peptide library of claim 134, wherein for each peptide of the family, X<sup>7</sup>  
2 independently is R or G.

1           142. The peptide library of claim 134, wherein for each peptide of the family, X<sup>8</sup>  
2 independently is T, A, or V.

1           143. The peptide library of claim 134, wherein for each peptide of the family, X<sup>9</sup>  
2 independently is Y or F.

1           144. The peptide library of claim 134, wherein for each peptide of the family, X<sup>10</sup>  
2 independently is A or T.

1           145. The peptide library of claim 134, wherein for each peptide of the family, X<sup>11</sup>  
2 independently is G, N, D, K or T.

1           146. The peptide library of claim 134, wherein for each peptide of the family, X<sup>12</sup>  
2 independently is D, G, N, S, or I.

1           147. The peptide library of claim 134, wherein for each peptide of the family, X<sup>13</sup>  
2 independently is I or T.

1           148. The peptide library of claim 134, wherein for each peptide of the family, X<sup>14</sup>  
2 independently is D or N.

1           149. The peptide library of claim 134, wherein for each peptide of the family, X<sup>15</sup>  
2 independently is Q, K, E, L or H.

1           150. The peptide library of claim 134, wherein for each peptide of the family, X<sup>16</sup>  
2 independently is H, Y, or N.

1 151. The peptide library of claim 134, wherein for each peptide of the family, X<sup>17</sup>  
2 independently is N, T, I, D or H.

1 152. The peptide library of claim 134, wherein for each peptide of the family, X<sup>1</sup>  
2 independently is V, N, E, T, M or R; X<sup>2</sup> independently is T, I, or A; X<sup>3</sup> independently is N,  
3 G, S, or H; X<sup>4</sup> independently is K, E or Q; X<sup>5</sup> independently is S or G; X<sup>6</sup> independently is I  
4 or M; X<sup>7</sup> independently is R or G; X<sup>8</sup> independently is T, A, or V; X<sup>9</sup> independently is Y or  
5 F; X<sup>10</sup> independently is A or T; X<sup>11</sup> independently is G, N, D, K or T; X<sup>12</sup> independently is  
6 D, G, N, S, or I; X<sup>13</sup> independently is I or T; X<sup>14</sup> independently is D or N; X<sup>15</sup> independently  
7 is Q, K, E, L or H; X<sup>16</sup> independently is H, Y, or N; and X<sup>17</sup> independently is N, T, I, D or H.

1 153. The peptide library of claim 134, wherein at least two members of the family  
2 of peptides are mixed together.

1 154. The peptide library of claim 134, wherein the family of peptides are separated  
2 according to sequence.

1 155. The peptide library of claim 134, wherein the family includes greater than 150  
2 mutually unique peptide sequences.

1 156. The peptide library of claim 134, wherein the family includes fewer than  
2 100,000 mutually unique peptide sequences.

1 157. The peptide library of claim 134, wherein the family includes fewer than 500  
2 mutually unique peptide sequences, the sequences being representative of the entire sequence  
3 diversity available.

1 158. A peptide library comprising a family of peptides including the fragment:  
2 -R-P-X<sup>3</sup>-X<sup>4</sup>-X<sup>5</sup>-X<sup>6</sup>-R-X<sup>7</sup>-X<sup>8</sup>-X<sup>9</sup>-X<sup>10</sup>-I-G-X<sup>11</sup>-G-X<sup>12</sup>-X<sup>13</sup>-X<sup>14</sup>-X<sup>15</sup>-X<sup>16</sup>-T-X<sup>17</sup>-X<sup>18</sup>-G-X<sup>19</sup>-I-  
3 wherein each X<sup>3</sup>-X<sup>19</sup> is a fragment zero, one, two or three amino acid residues in length.

1 159. The peptide library of claim 158, wherein the family has antigenic similarity  
2 to the V3 region of HIV gp120.

1           160. The peptide library of claim 159, wherein the family has antigenic similarity  
2 to the V3 region of HIV gp120 of subtype D.

1           161. The peptide library of claim 158, wherein the family of peptides have the  
2 formula:

3            $X^1-C-X^2-R-P-X^3-X^4-X^5-X^6-R-X^7-X^8-X^9-X^{10}-I-G-X^{11}-G-X^{12}-X^{13}-X^{14}-X^{15}-X^{16}-T-X^{17}-X^{18}-G-X^{19}-I-X^{20}-$   
4  $X^{21}-A-X^{22}-C-X^{23}$

5 wherein each  $X^1-X^{23}$  is a fragment zero, one, two or three amino acid residues in length.

1           162. The peptide library of claim 161, wherein for each peptide of the family,  $X^1$   
2 independently is N or T.

1           163. The peptide library of claim 161, wherein for each peptide of the family,  $X^2$   
2 independently is T or I.

1           164. The peptide library of claim 161, wherein for each peptide of the family,  $X^3$   
2 independently is Y or N.

1           165. The peptide library of claim 161, wherein for each peptide of the family,  $X^4$   
2 independently is N or K.

1           166. The peptide library of claim 161, wherein for each peptide of the family,  $X^5$   
2 independently is N or K.

1           167. The peptide library of claim 161, wherein for each peptide of the family,  $X^6$   
2 independently is T, I or K.

1           168. The peptide library of claim 161, wherein for each peptide of the family,  $X^7$   
2 independently is Q or R.

1           169. The peptide library of claim 161, wherein for each peptide of the family,  $X^8$   
2 independently is S, R or G.

1           170. The peptide library of claim 161, wherein for each peptide of the family,  $X^9$   
2 independently is T or I.



1           171. The peptide library of claim 161, wherein for each peptide of the family, X<sup>10</sup>  
2 independently is H, P, S or R.

1           172. The peptide library of claim 161, wherein for each peptide of the family, X<sup>11</sup>  
2 independently is P, L, S or Q.

1           173. The peptide library of claim 161, wherein for each peptide of the family, X<sup>12</sup>  
2 independently is Q or R.

1           174. The peptide library of claim 161, wherein for each peptide of the family, X<sup>13</sup>  
2 independently is A or T.

1           175. The peptide library of claim 161, wherein for each peptide of the family, X<sup>14</sup>  
2 independently is L or Y.

1           176. The peptide library of claim 161, wherein for each peptide of the family, X<sup>15</sup>  
2 independently is Y or F.

1           177. The peptide library of claim 161, wherein for each peptide of the family, X<sup>16</sup>  
2 independently is T or A.

1           178. The peptide library of claim 161, wherein for each peptide of the family, X<sup>17</sup>  
2 independently is I or K.

1           179. The peptide library of claim 161, wherein for each peptide of the family, X<sup>18</sup>  
2 independently is I, T or K.

1           180. The peptide library of claim 161, wherein for each peptide of the family, X<sup>19</sup>  
2 independently is D or N.

1           181. The peptide library of claim 161, wherein for each peptide of the family, X<sup>20</sup>  
2 independently is R or G.

1           182. The peptide library of claim 161, wherein for each peptide of the family, X<sup>21</sup>  
2 independently is Q or K.

1 183. The peptide library of claim 161, wherein for each peptide of the family, X<sup>22</sup>  
2 independently is H or Y.

1 184. The peptide library of claim 161, wherein for each peptide of the family, X<sup>23</sup>  
2 independently is N, T or K.

1 185. The peptide library of claim 161, wherein for each peptide of the family, X<sup>1</sup>  
2 independently is N or T; X<sup>2</sup> independently is T or I; X<sup>3</sup> independently is Y or N; X<sup>4</sup>  
3 independently is N or K; X<sup>5</sup> independently is N or K; X<sup>6</sup> independently is T, I or K; X<sup>7</sup>  
4 independently is Q or R; X<sup>8</sup> independently is S, R or G; X<sup>9</sup> independently is T or I; X<sup>10</sup>  
5 independently is H, P, S or R; X<sup>11</sup> independently is P, L, S or Q; X<sup>12</sup> independently is Q or R;  
6 X<sup>13</sup> independently is A or T; X<sup>14</sup> independently is L or Y; X<sup>15</sup> independently is Y or F; X<sup>16</sup>  
7 independently is T or A; X<sup>17</sup> independently is I or K; X<sup>18</sup> independently is I, T or K; X<sup>19</sup>  
8 independently is D or N; X<sup>20</sup> independently is R or G; X<sup>21</sup> independently is Q or K; X<sup>22</sup>  
9 independently is H or Y; and X<sup>23</sup> independently is N, T or K.

1 186. The peptide library of claim 161, wherein at least two members of the family  
2 of peptides are mixed together.

1 187. The peptide library of claim 161, wherein the family of peptides are separated  
2 according to sequence.

1 188. The peptide library of claim 161, wherein the family includes greater than 150  
2 mutually unique peptide sequences.

1 189. The peptide library of claim 161, wherein the family includes fewer than  
2 100,000 mutually unique peptide sequences.

1 190. The peptide library of claim 161, wherein the family includes fewer than 500  
2 mutually unique peptide sequences, the sequences being representative of the entire sequence  
3 diversity available.

1 191. A peptide library comprising a family of peptides including the fragment:  
2 -N-N-X<sup>3</sup>-R-K-X<sup>4</sup>-I-X<sup>5</sup>-L-G-P-G-X<sup>6</sup>-X<sup>7</sup>-X<sup>8</sup>-X<sup>9</sup>-X<sup>10</sup>-X<sup>11</sup>-X<sup>12</sup>-X<sup>13</sup>-I-X<sup>14</sup>-G-X<sup>15</sup>-I-R-  
3 wherein each X<sup>3</sup>-X<sup>15</sup> is a fragment zero, one, two or three amino acid residues in length.

1           192. The peptide library of claim 191, wherein the family has antigenic similarity  
2 the V3 region of HIV gp120.

1           193. The peptide library of claim 192, wherein the family has antigenic similarity  
2 the V3 region of HIV gp120 of HIV subtype F.

1           194. The peptide library of claim 191, wherein the family of peptides have the  
2 formula:

3            $X^1\text{-C-T-R-P-X}^2\text{-N-N-X}^3\text{-R-K-X}^4\text{-I-X}^5\text{-L-G-P-G-X}^6\text{-X}^7\text{-X}^8\text{-X}^9\text{-X}^{10}\text{-X}^{11}\text{-X}^{12}\text{-X}^{13}\text{-I-X}^{14}\text{-G-X}^{15}\text{-I-R-X}^{16}\text{-}$   
4  $\text{A-X}^{17}\text{-C-X}^{18}$

5 wherein each  $X^1\text{-X}^{18}$  is a fragment zero, one, two or three amino acid residues in length.

1           195. The peptide library of claim 194, wherein for each peptide of the family,  $X^1$   
2 independently is N or T.

1           196. The peptide library of claim 194, wherein for each peptide of the family,  $X^2$   
2 independently is N or S.

1           197. The peptide library of claim 194, wherein for each peptide of the family,  $X^3$   
2 independently is T or I.

1           198. The peptide library of claim 194, wherein for each peptide of the family,  $X^4$   
2 independently is S, G, or R.

1           199. The peptide library of claim 194, wherein for each peptide of the family,  $X^5$   
2 independently is H, R, Q, P, Y, or S.

1           200. The peptide library of claim 194, wherein for each peptide of the family,  $X^6$   
2 independently is Q, R or H.

1           201. The peptide library of claim 194, wherein for each peptide of the family,  $X^7$   
2 independently is A, V or T.

1           202. The peptide library of claim 194, wherein for each peptide of the family,  $X^8$   
2 independently is F or I.

1           203. The peptide library of claim 194, wherein for each peptide of the family, X<sup>9</sup>  
2 independently is Y, H or F.

1           204. The peptide library of claim 194, wherein for each peptide of the family, X<sup>10</sup>  
2 independently is A or T.

1           205. The peptide library of claim 194, wherein for each peptide of the family, X<sup>11</sup>  
2 independently is T or A.

1           206. The peptide library of claim 194, wherein for each peptide of the family, X<sup>12</sup>  
2 independently is G, D or S.

1           207. The peptide library of claim 194, wherein for each peptide of the family, X<sup>13</sup>  
2 independently is D, A, or N.

1           208. The peptide library of claim 194, wherein for each peptide of the family, X<sup>14</sup>  
2 independently is I or T.

1           209. The peptide library of claim 194, wherein for each peptide of the family, X<sup>15</sup>  
2 independently is D or N.

1           210. The peptide library of claim 194, wherein for each peptide of the family, X<sup>16</sup>  
2 independently is K or Q.

1           211. The peptide library of claim 194, wherein for each peptide of the family, X<sup>17</sup>  
2 independently is H or Y.

1           212. The peptide library of claim 194, wherein for each peptide of the family, X<sup>18</sup>  
2 independently is N, I, D, or K.

1           213. The peptide library of claim 194, wherein for each peptide of the family, X<sup>1</sup>  
2 independently is N or T; X<sup>2</sup> independently is N or S; X<sup>3</sup> independently is T or I; X<sup>4</sup>  
3 independently is S, G, or R; X<sup>5</sup> independently is H, R, Q, P, Y, or S; X<sup>6</sup> independently is Q,  
4 R or H; X<sup>7</sup> independently is A, V or T; X<sup>8</sup> independently is F or I; X<sup>9</sup> independently is Y, H  
5 or F; X<sup>10</sup> independently is A or T; X<sup>11</sup> independently is T or A; X<sup>12</sup> independently is G, D or

6 S; X<sup>13</sup> independently is D, A, or N; X<sup>14</sup> independently is I or T; X<sup>15</sup> independently is D or N;  
 7 X<sup>16</sup> independently is K or Q; X<sup>17</sup> independently is H or Y; and X<sup>18</sup> independently is N, I, D,  
 8 K or X.

1 214. The peptide library of claim 194, wherein at least two members of the family  
 2 of peptides are mixed together.

1 215. The peptide library of claim 194, wherein the family of peptides are separated  
 2 according to sequence.

1 216. The peptide library of claim 194, wherein the family includes greater than 150  
 2 mutually unique peptide sequences.

1 217. The peptide library of claim 194, wherein the family includes fewer than  
 2 100,000 mutually unique peptide sequences.

1 218. The peptide library of claim 194, wherein the family includes fewer than 500  
 2 mutually unique peptide sequences, the sequences being representative of the entire sequence  
 3 diversity available.

1 219. A peptide library comprising a family of peptides including the fragment:  
 2 -N-N-T-R-K-S-X<sup>4</sup>-X<sup>5</sup>-X<sup>6</sup>-G-X<sup>7</sup>-X<sup>8</sup>-X<sup>9</sup>-X<sup>10</sup>-X<sup>11</sup>-X<sup>12</sup>-X<sup>13</sup>-T-X<sup>14</sup>-I-X<sup>15</sup>-G-X<sup>16</sup>-I-R-  
 3 wherein each X<sup>4</sup>-X<sup>16</sup> is a fragment zero, one, two or three amino acid residues in length.

1 220. The peptide library of claim 219, wherein the family has antigenic similarity  
 2 to the V3 region of HIV gp120.

1 221. The peptide library of claim 220, wherein the family has antigenic similarity  
 2 to the V3 region of HIV gp120 of HIV subtype G.

1 222. The peptide library of claim 219, wherein the family of peptides have the  
 2 formula:

3 X<sup>1</sup>-C-X<sup>2</sup>-R-P-X<sup>3</sup>-N-N-T-R-K-S-X<sup>4</sup>-X<sup>5</sup>-X<sup>6</sup>-G-X<sup>7</sup>-X<sup>8</sup>-X<sup>9</sup>-X<sup>10</sup>-X<sup>11</sup>-X<sup>12</sup>-X<sup>13</sup>-T-X<sup>14</sup>-I-X<sup>15</sup>-G-X<sup>16</sup>-I-R-X<sup>17</sup>-  
 4 A-X<sup>18</sup>-C-X<sup>19</sup>

5 wherein each X<sup>1</sup>-X<sup>19</sup> is a fragment zero, one, two or three amino acid residues in length.

1           223. The peptide library of claim 222, wherein for each peptide of the family, X<sup>1</sup>  
2 independently is N, I, T, M or R.

1           224. The peptide library of claim 222, wherein for each peptide of the family, X<sup>2</sup>  
2 independently is T or I.

1           225. The peptide library of claim 222, wherein for each peptide of the family, X<sup>3</sup>  
2 independently is N or S.

1           226. The peptide library of claim 222, wherein for each peptide of the family, X<sup>4</sup>  
2 independently is I or K.

1           227. The peptide library of claim 222, wherein for each peptide of the family, X<sup>5</sup>  
2 independently is T, R, H, P or N.

1           228. The peptide library of claim 222, wherein for each peptide of the family, X<sup>6</sup>  
2 independently is F or I.

1           229. The peptide library of claim 222, wherein for each peptide of the family, X<sup>7</sup>  
2 independently is P, T, or L.

1           230. The peptide library of claim 222, wherein for each peptide of the family, X<sup>8</sup>  
2 independently is G or R.

1           231. The peptide library of claim 222, wherein for each peptide of the family, X<sup>9</sup>  
2 independently is Q, R, H or G.

1           232. The peptide library of claim 222, wherein for each peptide of the family, X<sup>10</sup>  
2 independently is A, T or V.

1           233. The peptide library of claim 222, wherein for each peptide of the family, X<sup>11</sup>  
2 independently is F, I or S.

1           234. The peptide library of claim 222, wherein for each peptide of the family, X<sup>12</sup>  
2 independently is Y or H.

1           235. The peptide library of claim 222, wherein for each peptide of the family, X<sup>13</sup>  
2 independently is A or T.

1           236. The peptide library of claim 222, wherein for each peptide of the family, X<sup>14</sup>  
2 independently is G, D or S.

1           237. The peptide library of claim 222, wherein for each peptide of the family, X<sup>15</sup>  
2 independently is I or T.

1           238. The peptide library of claim 222, wherein for each peptide of the family, X<sup>16</sup>  
2 independently is D or N.

1           239. The peptide library of claim 222, wherein for each peptide of the family, X<sup>17</sup>  
2 independently is Q, L, K or P.

1           240. The peptide library of claim 222, wherein for each peptide of the family, X<sup>18</sup>  
2 independently is H, Y or F.

1           241. The peptide library of claim 222, wherein for each peptide of the family, X<sup>19</sup>  
2 independently is N, K or T.

1           242. The peptide library of claim 222, wherein for each peptide of the family, X<sup>1</sup>  
2 independently is N, I, T, M or R; X<sup>2</sup> independently is T or I; X<sup>3</sup> independently is N or S; X<sup>4</sup>  
3 independently is I or K; X<sup>5</sup> independently is T, R, H, P or N; X<sup>6</sup> independently is F or I; X<sup>7</sup>  
4 independently is P, T, or L; X<sup>8</sup> independently is G or R; X<sup>9</sup> independently is Q, R, H or G;  
5 X<sup>10</sup> independently is A, T or V; X<sup>11</sup> independently is F, I or S; X<sup>12</sup> independently is Y or H;  
6 X<sup>13</sup> independently is A or T; X<sup>14</sup> independently is G, D or S; X<sup>15</sup> independently is I or T; X<sup>16</sup>  
7 independently is D or N; X<sup>17</sup> independently is Q, L, K or P; X<sup>18</sup> independently is H, Y or F;  
8 X<sup>19</sup> independently is N, K or T.

1           243. The peptide library of claim 222, wherein at least two members of the family  
2 of peptides are mixed together.

1           244. The peptide library of claim 222, wherein the family of peptides are separated  
2 according to sequence.

1           245. The peptide library of claim 222, wherein the family includes greater than 150  
2 mutually unique peptide sequences.

1           246. The peptide library of claim 222, wherein the family includes fewer than  
2 100,000 mutually unique peptide sequences.

1           247. The peptide library of claim 222, wherein the family includes fewer than 500  
2 mutually unique peptide sequences, the sequences being representative of the entire sequence  
3 diversity available.

1           248. A method of eliciting an immune response in a subject comprising  
2 administering to the subject a composition including a family of antigenic peptides having  
3 amino acid sequences having antigenic similarity to amino acid sequences of a variable  
4 region of a pathogen protein of a pathogen.

1           249. The method of claim 248, wherein the antigenic similarity is determined using  
2 an antigenic similarity matrix.

1           250. The method of claim 248, wherein the composition is administered to a  
2 subject prior to infection by the pathogen.

1           251. The method of claim 250, wherein the family of antigenic peptides has amino  
2 acid sequences having antigenic similarity to amino acid sequences of a subtype of the  
3 pathogen protein.

1           252. The method of claim 250, wherein the family of antigenic peptides has amino  
2 acid sequences having antigenic similarity to amino acid sequences from more than one  
3 subtype of the pathogen protein.

1           253. The method of claim 248, wherein the composition is administered to a  
2 subject infected by the pathogen.

1           254. The method of claim 253, wherein the subject is infected by a subtype of the  
2 pathogen.



1           255. The method of claim 254, wherein the family of antigenic peptides has amino  
2 acid sequences having antigenic similarity to amino acid sequences from the subtype by  
3 which the subject is infected.

1           256. A method of designing a family of peptide sequences, comprising:  
2 locating a plurality of variable positions in a region of a pathogen protein;  
3 choosing a peptide sequence of the pathogen protein including the variable positions;  
4 and  
5 selecting one or more substitute amino acid residues for one of the variable positions  
6 of the peptide based on antigenic similarity to amino acid residues naturally occurring at the  
7 variable position of the pathogen protein, thereby forming a family of peptide sequences.

1           257. The method of claim 256, wherein selecting includes determining the  
2 antigenic similarity using an antigenic similarity matrix.

1           258. The method of claim 256, further comprising assigning a frequency to each  
2 substitute amino acid residue in the family of antigenic peptide sequences.

1           259. The method of claim 258, wherein assigning further includes considering the  
2 frequency with which the variations naturally occur.

1           260. The method of claim 256, further comprising determining an antigenic  
2 similarity between a peptide of the family and a region of a human protein.

1           261. The method of claim 260, further comprising removing a peptide sequence  
2 from the family of peptide sequences if the calculated antigenic similarity between the  
3 peptide of the family and the region of a human protein exceeds a predetermined threshold.

1           262. The method of claim 256, wherein the family of peptide sequences includes  
2 members, such that the members taken together have antigenic similarity to each naturally  
3 occurring sequence of the region of the pathogen protein.

1           263. The method of claim 256, wherein the family of antigenic peptides includes  
2 members, such that the members taken together have antigenic similarity to a non-naturally  
3 occurring sequence of the region of the pathogen protein.

1           264. The method of claim 256, further comprising identifying peptide sequences of  
2 the family, the identified peptide sequences being representative of the sequence diversity of  
3 the entire family.

1           265. The method of claim 264, wherein fewer than 500 sequences are identified.

1           266. The method of claim 264, wherein identifying includes calculating a distance  
2 between peptide sequences of the family.

1           267. The method of claim 266, wherein calculating a distance includes using an  
2 antigenic similarity matrix.

1           268. The method of claim 256, further comprising identifying peptide sequences of  
2 the family having antigenic similarity to a subtype of the pathogen protein.

1           269. The method of claim 256, wherein the pathogen protein includes a  
2 hypervariable region.

1           270. The method of claim 256, wherein the pathogen is a virus.

1           271. The method of claim 270, wherein the virus is HIV.

1           272. The method of claim 271, wherein the pathogen protein is gp120.

1           273. The method of claim 272, wherein the region is selected from the group  
2 consisting of the V1 region, the V2 region, the V3 region, the V4 region, and the V5 region.

1           274. A method of diagnosing infection comprising contacting a sample with a  
2 family of peptides having amino acid sequences having antigenic similarity to amino acid  
3 sequences of a variable region of a pathogen protein, wherein each peptide in the family has  
4 at least one amino acid position that varies relative to other peptides in the family.

1           275. The method of claim 274, wherein antigenic similarity is determined using an  
2 antigenic similarity matrix.

1           276. The method of claim 274, wherein the family of peptides is antigenically  
2 similar to a pathogen subtype.

1           277. The method of claim 274, wherein the family of peptides is antigenically  
2 similar to more than one pathogen subtype.

1           278. The method of claim 274, further comprising immobilizing the family of  
2 peptides on a substrate before contacting.

1           279. The method of claim 274, further comprising determining if the sample  
2 includes antibodies that bind specifically to the family of peptides.